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PRINCIPAL INVESTIGATOR: Mary Klein, Ph.D.

CONTRACTING ORGANIZATION: Albert Einstein Healthcare Network
Philadelphia, Pennsylvania 19141

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Mary Klein, Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Albert Einstein Healthcare Network
Philadelphia, Pennsylvania 19141

E-Mail: mklein@einstein.edu

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The goals of this project are: 1) to study the temporal relationship between activity level and health status in polio survivors and to compare the results with those obtained from an age-matched control population and 2) to look at the effect of localized muscle weakness and the associated compensation response on performance of a walking task. Simulation modeling techniques will be used to identify factors critical to task performance, which will provided valuable information for optimizing rehabilitation interventions for polio survivors and other populations with lower extremity muscle weakness. To date, a total of 83 polio survivors and 109 controls have been enrolled and tested for Study #1. Analysis of the longitudinal data is in progress. Data collection for Study #2 has begun. The functional deficits database is being compiled and preliminary analysis using the mechanical-based compensation scheme is underway.

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INTRODUCTION

Controversy exists regarding the relationship between strength, functional performance, and health status in the post-polio population, and the role of activity level in this relationship. Polio survivors tend to have a higher incidence of muscle and joint pain and higher levels of fatigue after normal daily activity compared to the general population. One possible explanation is that, because of their residual muscle weakness, polio survivors perform their activities at a higher activity intensity level than their peers, which may, in turn, make them more susceptible to musculoskeletal problems. However, there have not been any systematic studies performed to confirm this theory. Therefore, one of the goals of this project is to study the temporal relationship between activity level and health status in polio survivors and to compare the results with those obtained from an age-matched control population. A need also exists for improved neuromuscular, musculoskeletal, and link segment dynamic models of common daily activities that can be used to predict the compensatory strategies that will be employed when muscle weakness is present. Therefore, another goal of this research is to look at the effect of localized muscle weakness and the associated compensation response on performance of a walking task. Simulation modeling techniques will be used to identify factors critical to task performance, which will provide valuable information for optimizing rehabilitation interventions for polio survivors and other populations with lower extremity muscle weakness.

BODY

Study #1: An Analysis of Health Status and Activity Level in Polio Survivors Over Time

As of Sept. 10, 2004, a total of 191 subjects had completed at least one of the four required visits. Visit information is summarized in Table 1 and demographic information is listed in Table 2. Of the 83 polio survivors enrolled in the study so far, 72% reported symptoms of post-polio syndrome (PPS). However, only 63% of those subjects had been diagnosed with PPS by a physician. The average number of years since the original polio infection was 57.76 (8.09) years for all the post-polio survivors in this study.

When asked to rate their current health status on a scale from 0 (worst it could be) to 100 (best it could be), the average rating for the polio survivors was 74.64 (17.63). Twenty-eight percent (28%) of the polio survivors felt that their health status was improving overall, while 7% said their health status was decreasing and the remaining 65% reported no recent change in health. The majority of controls (79%) also reported that their health status remained pretty stable, with little or no change. However, sixteen percent (16%) of the controls reported their health status was improving and 5% reported a recent decrease in health status, which resulted in average health rating of 78.83 (14.71).

Preliminary data analysis of the longitudinal data from the first 86 subjects (38 polio survivors and 48 controls) to complete the first four visits is in progress. Originally, it was hypothesized that the severity ratings for both pain and fatigue would be higher among polio survivors than controls. However, an analysis of the pain ratings recorded for each day the monitor was worn

Table 1. Number of Subjects Who Completed Each Visit as of 9/10/03

Group	Visit 1	Visit 2	Visit 3	Visit 4
Post-polio	83	62	53	39
Control	109	82	69	52

Table 2. Descriptive Statistics

Variable	Post-Polio	Control
# enrolled	83	109
Gender	M-43, F-40	M-38, F-71
Age Range (yr)	38-81	49-90
Age (Mean(SD))	63.75 (9.1)	72.67 (8.88)
PACE score	155.37 (99.55)	152.97 (73.36)
FSS score	36.15 (15.09)	27.42 (11.16)
Strength (lb):		
Lt Peak Knee Ext.	32.16 (23.18)	44.92 (18.20)
Rt Peak Knee Ext.	31.00 (23.78)	41.57 (20.25)

showed no significant difference in average pain severity between groups ($p = 0.065$). There was also no evidence to indicate that polio survivors who have been diagnosed with PPS were more likely to report pain than those who had not been diagnosed with PPS ($p = 0.19$). However, there was a strong association between pain severity and body mass index ($p = 0.008$) with heavier people in both groups reporting more pain overall than smaller people. Neither gender nor age were significant factors.

With regard to fatigue, the Fatigue Severity Scale (FSS) ratings showed a significant group effect ($p = 0.028$), with polio survivors reporting higher levels of fatigue than controls. However, an analysis of the fatigue ratings recorded at home at the end of each day the monitor was worn showed no significant group difference ($p = 0.432$). These fatigue ratings are recorded at the end of each day and may have a closer association to daily activity levels than the baseline measure.

Both fatigue measures were strongly associated with knee extensor strength. As expected, weaker people reported higher levels of fatigue for both the FSS and the home fatigue measures.

Analysis of the step monitor data revealed that polio survivors were significantly less active than controls ($p = 0.001$). However, polio survivors had significantly higher ratings on the subjective activity measure (PASE) than controls ($p < 0.001$). This apparent contradiction will require some additional analysis before an explanation can be offered. Body mass index was also a significant factor. People who were bigger tended to be less active than those who were smaller.

Future data analysis will focus on changes over time in the pain, fatigue and activity measures. The results of the preliminary analysis for both the pain and fatigue measures indicated significant seasonal effects. In order to control for the seasonal effects, we will need to collect additional data on these subjects so that we have two sets of data for at least one season. The greater number of follow-up measurements per subject will greatly increase the statistical power of the study to detect small within-person and within-group changes over time in activity level and other outcomes. A request for a protocol modification that would allow for additional visits has been submitted to the HSRRB for review. New subjects are continuing to be recruited and we anticipate no problems in meeting the original study goals.

Study #2 Development of a Walking Model for Simulating the Effect of Localized Muscle Weakness

Administrative

1. As planned and budgeted in the original proposal, Dr. Talaty has begun interactions with a well established computer simulation group to learn and improve the model being used and to augment our level of technical sophistication. This interaction will help to ensure that adequate technical expertise will be infused into the project, since the overall amount and level of computer simulation experience at MossRehab initially raised a concern in the review panel. Initial technical inputs and interaction were conducted with Dr. Necip Berme (Professor, Ohio State University) who has considerable experience in modeling and computer simulation. This ensured the project conceptualization was reasonable, feasible and progressing as planned. The interaction with the currently active computer simulation group was begun in the later years of the project to ensure our group had developed substantial familiarity and working knowledge of the computer model being used for this project. In order to satisfy the initial concerns expressed by the review panel, an existing and developed external model was selected to be used in the simulation efforts rather than our group developing one *de novo*. Thus, it was necessary for us to learn how the model worked and to "reverse engineer" it to some degree – before we could transform and permute it to achieve the proposed project objectives. For this reason, it would have been less effective to interact with an established group until we were at least experts with our own model.

   A collaborative interaction has been defined with Dr. Ton van den Bogert of the Cleveland Clinic Foundation that will allow Dr. Talaty to spend time discussing and improving the current model. This will strongly contribute to our ability to complete all the project tasks in the highest technical manner. Dr. van den Bogert has over twenty

years of experience in computer simulation and is considered an expert in the field. For example, he has recently given an educational tutorial in computer simulation at an international biomechanics meeting (International Society of Biomechanics, Dunedin New Zealand, June 2003). He has published extensively (journal papers, book chapters) and continues to do so. It is noted that originally, Dr. Talaty intended to collaborate with the Anybody group in Denmark. For practical and scientific reasons, an interaction with Dr. van den Bogert will be more suitable and time and cost efficient. Substantially reduced travel expenses should allow better use of the research monies. A letter from Dr. van den Bogert formalizing our interactions is included in this report. In this letter, Dr. van den Bogert indicates his willingness to 1) learn and provide expert feedback about our CPG-based model and 2) to host Dr. Talaty giving access to his laboratory, learn his approaches, and utilize his tools. This interaction will ensure all current project deliverables are realized. Further, it is noted that this collaboration aims to continue the work Dr. Talaty has begun in the current project to quantify the role of disorder (i.e. muscle weakness) and to extend that work to be able to predict responses to intervention.

Interactions with project consultant, Professor Necip Berme of the Ohio State University, have been maintained as needed. Email and phone discussions have been exchanged periodically over the past twelve months.

Scientific & Technical

1. Human subject data collection was successfully completed for half of the required subjects (three out of the target six). No unusual or adverse events have been reported. Data analysis continues to quantify how the subjects' gait changed due to the induced weakness. Reliability analysis of the methods developed to gauge weakness was performed to ensure meaningful strength measurement methods were being used.

   The aim of this testing was to generate human data to compare to that of the model. One main goal of this computer simulation project is to determine how much of an individual's compensatory strategy for muscle weakness is driven by purely mechanical factors. The general paradigm was that temporary weakness would be introduced in a group of healthy normal subjects using Lidocaine injected into the muscle. Walking would be measured before and after the weakness was created. These human subject data would then be compared to the computer model in which muscle weakness was simulated.

   Human subject testing to date has been conducted without any surprises, unexpected or adverse events. Patients have reported zero side effects or even discomfort – and have usually not even indicated an awareness of being given the injection. A cold spray is used reduce sensations at the immediate injection site – as is standard protocol for clinical patients receiving neuromuscular blocks. These data are being analyzed to characterize how subjects responded to the block and how their walking pattern changed from their baseline to after muscle weakness was induced.

In order to be able to accurately gauge strength reduction due to the block, a reliable technique to quantify changes in strength using a hand-held dynamometer-assisted strength testing technique was established. Using the Reliability Assessment component of SPSS Statistical analysis software (SPSS10,), test – retest reliability of strength measurement protocol using the Microfet hand-held dynamometer (Microfet2 #5021, Hoggan Health Industries; Draper UT) was established. Reliability values established that the methods developed to measure muscle group (joint) strength for hip, knee and ankle joints ranged from 0.911 to 0.998 for the three subjects on whom assessment was performed.

2. The analysis to generate the functional deficits database was performed. Three different, but related, ways to assess the functional role of muscle were utilized. This analysis and interpretation is in progress; the database is being compiled.

   This database will give a qualitative and quantitative measure of the contribution of each muscle group to the motion it produced during walking. It was a project deliverable. To develop it, three approaches were employed. First, as proposed, the IDA (intersegmental dynamics analysis or induced acceleration analysis) techniques were used to quantify the contribution of each muscle group to the acceleration it produced at the key degrees of freedom during walking. Then, the accelerations, velocities, and displacements of each of these degrees of freedom during walking were compiled and reconciled to the contribution of each muscle group. In this way, the contribution of each muscle group could be placed in a meaningful context. Then, the differences in how the model produced walking compared to how a typical human did were noted as well. The second approach to understanding the functional contribution of muscle to the gait motion was by running open loop simulations with muscle weakness. It was expected that the model would not be able to maintain stability for a complete gait cycle in this scenario. This was indeed found to be the case. Open loop simulations were known to be very sensitive to the balance of forces existing during walking. Altering that force balance even slightly results in instability. However, it was expected to be able to run simulations for brief periods (<100ms or so) and then restart from the "correct" position at subsequent periods of the gait cycle. This analysis is still in progress. A final means to quantify the functional contribution of each muscle group to the walking movement was position analysis (or "induced position analysis" – as has recently been published to be an informative analysis tool. [Anderson et al. Contributions of muscle forces and toe-off kinematics to peak knee flexion during the swing phase or normal gait : an induced position analysis. Journal of Biomechanics, 37 (20044). 731-737].

   A brief overview of the factors involved with each method is now provided, to give an example of the types of issues the affect the interpretation of each data set. We are clarifying the impact of each of these issues on our interpretation of the data and ultimately to the development of the functional deficits database.

a. **IDA** uses actual data from the known walking profile to calculate an instantaneous contribution of each muscle group (net joint moment) to the acceleration it produces at each degree of freedom in the body. To do so, each moment is "applied" separately from all the others. In other words, one joint moment is applied – and all the other loads (joint moments, gravity, velocity) are removed. To check that such a calculation is accurate, the individual contributions of each independent loads are added together. The result should equal the known acceleration profile of the body obtained from movement analysis. The extent to which it does not is termed reconstruction error. These errors can be quite large in human subject data because the method to solve for joint moment, unconstrained inverse dynamics, can be quite inaccurate. Thus, the moments and motion they produce are not consistent. Because of this, the model data are used for this analysis. However, the model must produce the walking movement in as exact a means as the human. The baseline analysis performed in the first year of this project showed that this model produced walking in a very similar but not exact way as a "normal" human.

   A final issue with IDA is that it reports the contribution of joint moments to *acceleration*. Acceleration is not commonly evaluated in clinical practice nor do we have an intuitive notion of normal and pathological acceleration patterns in gait.

b. **Open loop simulations** avoid the issue of acceleration in that actual motions are produced. A muscle can be weakened, a simulation run, and the exact movement profile (displacements, joint angles, etc.) that results can be obtained. However, one problem with simulation is validation. Would the human system being modeled respond in the same way as the computer representation? Further, open loop simulations of human walking are notoriously unstable. Using small periods of time and resetting the simulation to the known body orientation can help to overcome this limitation and is being pursued. Again, the issue of having the computer model produce the walking in the same way is important. If in humans, the role of the plantarflexor group is to produce knee and trunk stability in early and midstance and to produce propulsion in late stance but in the model the plantarflexors act to extend the hip and brake forward propulsion in early stance, then trying to infer human ankle plantarflexion function from the model would not be particularly useful. A careful look at how the walking is produced in each is warranted.

c. **Induced position analysis** eliminates the shortcoming of needing to interpret acceleration and some of the difficulty of validating simulation. The basic paradigm is similar to the IDA described above. However, the acceleration profile calculated in IDA is numerically integrated to produce velocity and then integrated again to produce position. Thus, the contribution of the muscle group (joint moment) to the position of each degree of freedom in the body is calculated. Further, validation may be as simple as adding together the individual

contributions to final position. If the sum equals the known position, the validity of the analysis is supported. However, the limitation of the joint moments having the same role in the human and the model still remains. Further, as in IDA, errors in the basic inverse dynamics that contribute both to reconstruction errors and in errors in interpretation of muscle function exists.

Results and interpretations from all three analyses will be compared to corroborate each. This will provide a more robust means to clarify the role of each muscle group during walking. Interpretations of this data base are still underway. The most intuitive means to convey the information in the data base is being explored for subsequent presentation. Finally, these will be presented to the lab medical doctor – a physiatrist with extensive training in clinical gait analysis and data interpretation – for assessment of the possible importance of these data to clinical decision making. A journal paper draft based on these results has been written. It is anticipated to submit it for publication and reviewed in approximately 6-9 months.

3. A preliminary and small-scale optimization was implemented during the open loop simulation efforts. Optimization, an ancillary mathematical technique to our main project, was learned and implemented to assist in generating meaningful open loop simulations for the functional database objective. It is anticipated to be useful for the upcoming analysis to calculate the compensation scheme.

   Optimization was used to determine necessary values for certain parameters in an open loop forward dynamic simulation. Specifically, it was used to determine the initial velocity necessary to recreate a known movement profile of a single body segment when known but noisy and slightly modified forces were applied. The optimization technique selected was simulated annealing, due to its versatility and power in biomechanical applications. Such a technique may be required when weakness is introduced and a new control scheme is solved for on the basis of mechanical potential. Such an open loop simulation will likely be sensitive to noise and other numerical integration phenomenon, and so will require some subtle adjustment or tuning to perform as desired. Further efforts in this area have been undertaken through collaboration with Dr. Ton van den Bogert (see letter affirming his willingness to collaborate with our group). Dr. Ton van den Bogert of the Cleveland Clinic Foundation is an established researcher in the field of optimization and computer simulation. He has successfully used and published numerical optimization techniques in biomechanical walking simulations.

4. Implementation of mechanical-based compensation scheme has begun, the mathematical routines have been formalized and initial analyses have been run.

   Preliminary analyses have been begun by formalizing the conceptual mathematical framework to calculate how joint torques will be altered to predict a response pattern to focal weakness induced by the block. Matlab (The Mathworks, Natick MA) has been

selected as the platform for solving for the compensated torques. To do so requires solution of the over-determined system. In short, there are 5 joint torques (3 joints x 2 legs – 1 – the weakened joint) that can be varied to produce the same acceleration profile as the initial unweakened condition. There are nine degrees of freedom for which accelerations are calculated. Each torque can contribute to each degree of freedom. So the system is over-determined. Solution requires slightly different techniques than for a normal system in which the number of unknowns equals the number of equations. The Matlab "backslash" operator is a least squares technique – similar to generating a line of best fit. Doing so generates errors in the desired output quantities – the body accelerations. A single data run has been input and a solution has been obtained with compensated torques. Plugging these torques or accelerations into a forward dynamic solution give widely varying results. Further, a qualitative comparison of the computed compensated joint torques was made to one data trial of one human subject. The results were significantly different. Robustness and sensitivity of this over-determined solution technique to how the problem is posed, noise in the data and other mathematical factors is being evaluated.

KEY RESEARCH ACCOMPLISHMENTS:

- A total of 83 polio survivors and 109 controls have been enrolled in Study #1.
- Preliminary analysis of the longitudinal data in Study #1 is in progress.
- Data on three subjects have been collected for Study #2.
- The functional deficits database is being compiled.
- A preliminary and small-scale optimization system has been implemented.
- Preliminary analysis using the mechanical-based compensation scheme has begun.

REPORTABLE OUTCOMES:

- Dr. Talaty was invited to lecture at the 5th SIAMOC (Societa Italiana Di Analisi Del Movimento in Clinica) Congress, Loano, Italy 10/3-10/5 2004. His talk was entitled, "Models for Gait Analysis," and included some work completed on this project. The Department of the Army was acknowledged.
- Ms. Mausam Patel, one of the Research Assistants working on this project, completed her Master's Degree in June 2004 in Biomedical Engineering from the School of Biomedical Engineering, Science and Health Systems in Philadelphia; her thesis was entitled, "Evaluation of the Compensatory Response of a CPG-based Neuromuscular Skeletal Model to Localized Muscle Weakness." The Department of the Army was acknowledged.

CONCLUSIONS:

This section is not applicable at this time.

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Antonie J. van den Bogert, Ph.D.
Assistant Staff
Biomedical Engineering / ND20
Office 216/444-5566
Fax 216/444-9198
E-mail bogert@bme.ri.ccf.org

Mary Klein, PhD
Acting Director of Research and Technology Development
Albert Einstein Medical Center
Korman Suite 100
1200 West Tabor Road
Philadelphia, PA 19141

October 5, 2004

RE: Collaboration with Dr. Mukul Talaty

Dear Ms. Klein,

This letter is to let you know that I am seeking a formal collaboration with Dr. Mukul Talaty at the Moss Rehabilitation Research Institute.

Dr. Talaty and I have been communicating in recent months in order to develop a collaborative research project on neuromechanical modeling of movement disorders. My laboratory at the Cleveland Clinic has developed detailed biomechanical models, and Dr. Talaty has developed computational models with detailed representation of neural mechanisms, but with simpler biomechanics. We intend to merge the two technologies in order to come up with a realistic computational model that can predict the effect of clinical interventions on the movement of a patient with a movement disorder.

The preliminary work has progressed well, independently in the two laboratories, and we are now at the stage that we wish to spend some time together to learn about each other's research tools. I would like to gain familiarity with Dr. Talaty's CPG-based models, and I would like to invite Dr. Talaty to my laboratory to learn how to use my models and software tools. This preliminary collaborative work will be incorporated in a joint NIH grant proposal that combines the unique strengths of both laboratories.

Regards,

Antonie J. (Ton) van den Bogert